## REMARKS

The Office Action mailed April 27, 1999, has been received and its contents carefully noted. The applicants acknowledge with thanks the Examiner's decision to allow claims 1, 3, 4, 20, 23, and 26.

The examiner has identified the following issues in the current application:

1. Informalities in the abstract.
2. The oath is defective.
3. Claims rejected under 35 U.S.C.§112, second paragraph for:
    a. lack of SEQ ID NO.s.
    b. lack of clarity as to the form,
    c. failure to define terms,
    d. grammatical errors,
    e. indefiniteness.
4. Claims 12, 17, and 18 were rejected under 35 U.S.C. §112, first paragraph, for lack of enablement and claim 14 was rejected failure to identify where and when of material was deposited so as to enable it use.

The applicants respectfully request reconsideration and withdrawal of all outstanding rejections in view of the preceding amendments and the remarks that follow.

A new Abstract has been added to the Application and has been reproduced on a separate sheet attached hereto.

The applicants respectfully submit that the supplemental declaration is not defective. The inventors used the form day, month, year, with the month, October, being indicated by the Roman numeral X and the day being indicated by the Arabic numeral 8, thus the declaration was signed on October 8, 1998. The supplemental declaration supplements the original declaration

with respect to the French Priority application and refers to the case by the attorney docket number, refers to the application by the title and international application number and was accompanied by a transmittal letter providing all particulars. The applicants submit that this is an acceptable supplemental declaration and needs no correction.

Claims 5, 6, 11, 13, 15, 16, and 25 have been amended according to the Examiner's recommendation to correct errors in grammar and diction.

Claims 2 and 22 have been amended to include SEQ ID NO:s for four amino acid sequences, SEQ ID NO:s 7 through 10. The sequence listing will be prepared and submitted in due time. The Examiner further requested SEQ ID NO:s for the amino acids 498, 510, 185, and 199. The applicants respectfully submit that the last four positions are not referred to in the rejected claims.

The Examiner has rejected claims 7 and 11 because they use the term " vaccinating antigen." The applicant herein submits pages from *The Dictionary of Science and Technology,* Academic Press, which define vaccinate and antigen. The applicants respectfully submit that, in light of their dictionary definitions, these terms would be understood by one of skill in the art as meaning an antigen useful in vaccination to induce an immune response and thus produce resistance to disease or infection in humans or animals.

The Examiner has rejected claims 8 and 10 as being indefinite because they use the term "therapeutic enzyme." The applicant respectfully submits that the term is defined in the specification on page 6, line 25, in the paragraph numbered iv). The applicant further asserts that the term was current in the art at the time that the application was filed. In support of this assertion the applicant references the publication: K.W. Culver, *et al.* (1992) Science, 256:1550, in which thymidine kinase is described as a therapeutic enzyme that is widely used in suicide gene therapy. Enzymatic proteins or enzymes are also frequently used or contemplated as

therapeutic substances to prevent or cure metabolic disorders. Lipases, abzymes, Rnases, are some of the well-known therapeutic enzymes.

The Examiner has rejected claim 9 as being indefinite because it contains the term "CD4 derivative" which was not defined in the specification. The applicant respectfully submits that the term "CD4" and "CD4 derivative" were well known in the art at the time the application was filed. CD4 derivatives are molecules that incorporate CD4 sequence or fragment thereof, or modification thereof and that retain the ligand property of the native CD4 molecule. The understanding of the word "derivative" was generally recognized in the scientific community in so far as the definition is a part of the Uniform Biological Material Transfer Agreement, published in the Federal Register on March 8, 1995. The applicants believe that the agreement of the scientific community as to the definitions of "derivatives" or functional equivalents for the establishment of ownership of intellectual property rights establishes the meaning of the term.

The Examiner has rejected claims 10 and 12 as being indefinite because it is not clear what a "ligand property" includes. The applicant submits that the term "ligand property" was well known in the art and generally accepted to characterize the functional property of the ligand, i.e., its specificity and its affinity. Thus the words are used in their usual meaning in the field.

The Examiner has rejected claim 17, because the term "medicament" does not further limit claim 1, from which it depends. The applicants have changed the claim to substitute "pharmaceutical composition" for "medicament" which better captures the intent of the applicant to include the possibility of combining the polypeptide of claim 1 with pharmaceutical carriers, excipients, or other ingredients. The term "pharmaceutical composition" is so used in the specification on page 9, line 36.

The rejection of claims 12, 17, and 18 under 35 U.S.C. §112, first paragraph, have been obviated by the amendments made herein to claims in view of the arguments which follow.

The Examiner has rejected claims 12, 17, and 18 as not being enabled by the specification in that there is no enablement for uses in therapy or prophylaxis of foetomaternal alloimmunization, viral, bacterial or parasitic infections, disseminated lupus erythematosus, or other alloimmune or autoimmune diseases. The applicants respectfully submit that the molecules originate from a normal plasma molecule and their biological properties are derived from this molecule. Their properties are predictable from the known functions of the parent molecules and from experimental information that was published at the time the application was filed.

The expected therapeutic potentialities of these heteromultimeric molecules are demonstrated by experiments wherein a chimeric recombinant multimeric CD4 was constructed by merging the sequence encoding the extracellular CD4 to the C terminal sequence encoding C4bp. Multimeric CD4 was secreted as an hexamer, bound by HIV gp120, and efficiently inhibited *in vitro* HIV infection. Implantation in nude mice of CD4-C4bp secreting cells led to stable homogeneous multimers accumulating for weeks. Briefly 293 cells were transfected using calcium phosphate precipitation method, by mono CD4, CD4-C4bp, or CD4-HAS C4bp αPCI vectors obtained by the method described in the article by Shinya, *et al.*, which is enclosed as Exhibit 5.

The 293 clones secreting multi-CD4, mono-CD4, CD4-HAS or non-transfected 293 cells were used to prepare organoids. Organoids containing $5 \times 10^5$ 293 cells each, were surgically implanted into the peritoneal cavity of 6-week Swiss (nu/nu) nude mice (Iffa-Credo, France) Neo-organ formation, implantation, and removal were performed as described in Valere, T. et al., (1995) Gene Therapy, 2:197-202. The results are shown figure 3 of Shinya, *et al.*, Exhibit 5 and the figure of Exhibit 6. In these experiments the nude mice, which produced CD4-C4bp multimeric molecules, were able to inhibit HIV infection , see figure 2 of Shinya, *et al.*, Exhibit 5.

Moreover, the applicants believe these therapeutic results are predictable from the disclosure of the invention. The molecules have retained their normal functions, which were well known in the art. The molecules of the invention combine these known functions in novel and useful ways, but the functions are predictable. Exhibit 7 shows the results of an experiment using a chimeric fusion protein of CD46 and C4bpα, which inhibits measles infection. This was co-injected with virus, it selectively inhibited measles infection but not canine distemper virus infection. Information in support of the above arguments has been provided in the for of Exhibits 5, 6, and 7. If the Examiner finds this information necessary for his decision, they can be provided in the form of a 37 C.F.R. 1.132 Declaration.

Thus, the claimed therapeutic effect of the claimed fusion protein is predictable and can be deduced from the function of these heterologous proteins.

With respect to the Examiner's enquiry concerning the deposit of material; the material has been deposited according to the terms of the Budapest Treaty. A Declaration, signed by the applicant, that identifies the place and date of the deposit is submitted with this amendment.

Enclosed herewith is an Information Disclosure Statement providing documents referenced above.

In view of the foregoing amendments and remarks, it is requested that the rejections of record be reconsidered and withdrawn, that claims 2, 5, 6, 11, 13, 15, 16, 17, 22, and 25 as amended, be allowed in addition to allowed claims 1, 3, 4, 20, 23, and 26, and that the Application be found to be in allowable condition.

Should the Examiner not find the Application to be in allowable condition or believe that a conference would be of value in expediting the prosecution of the Application, Applicants request that the Examiner telephone undersigned Counsel to discuss the case and afford Applicants an opportunity to submit any Supplemental Amendment that might advance prosecution and place the Application in allowable condition.


Respectfully submitted,

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Enclosures( 4)